

~~TOXIC HAZARDS DIVISION~~
~~TOXIC HAZARDS DIVISION~~

AMRL-TR-64-106

AD 608 841

PYRIDOXINE (VITAMIN B₆) TOXICITY LITERATURE REVIEW

ROBERT A. SCHNEIDER, CAPTAIN, USAF, MC, FS
RESIDENT, AVIATION MEDICINE, PHASE III

OCTOBER 1964

20060706032

STINFO COPY

PHYSIOLOGY DIVISION
BIOMEDICAL LABORATORY
AEROSPACE MEDICAL RESEARCH LABORATORIES
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related government procurement operation, the government thereby incurs no responsibility nor any obligation whatsoever; and the fact that the government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

Qualified requesters may obtain copies from the Defense Documentation Center (DDC), Cameron Station, Alexandria, Virginia 22314. Orders will be expedited if placed through the librarian or other person designated to request documents from DDC (formerly ASTIA).

Do not return this copy. Retain or destroy.

Stock quantities available, for sale to the public, from the Office of Technical Services, Department of Commerce, Washington, D. C. 20230.

Change of Address

Organizations and individuals receiving reports via the Aerospace Medical Research Laboratories automatic mailing lists should submit the addressograph plate stamp on the report envelope or refer to the code number when corresponding about change of address.

**PYRIDOXINE (VITAMIN B₆) TOXICITY
LITERATURE REVIEW**

*ROBERT A. SCHNEIDER, CAPTAIN, USAF, MC, FS
RESIDENT, AVIATION MEDICINE, PHASE III*

FOREWORD

This literature review was performed at the suggestion of the Biomedical Laboratory of the Aerospace Medical Research Laboratories, Toxic Hazards Branch, Physiology Division, Wright-Patterson Air Force Base, Ohio, and in partial fulfillment of the Phase III requirements for residency in Aviation Medicine. Sponsors for this portion of the work were Dr. Anthony Thomas and Dr. Kenneth Back, Toxic Hazards Branch.

This technical report has been reviewed and is approved.

WAYNE H. McCANDLESS
Technical Director
Biomedical Laboratory

ABSTRACT

The literature from 1940 through June 1963 was surveyed to summarize the data from pyridoxine toxicity studies in animals and to ascertain the highest doses of pyridoxine (vitamin B₆ analogs) that have been administered to human subjects as a therapeutic measure with no clinical evidence of toxicity. Analysis of the data indicated that doses of 25 mg/kg pyridoxine hydrochloride should be well tolerated as a therapeutic measure when required. In particular, pyridoxine hydrochloride can be used when required in the specific treatment of a clinical entity such as acute UDMH intoxication.

SECTION I

INTRODUCTION

The increased use of 1,1-dimethylhydrazine (UDMH) as a missile propellant in recent years has necessitated numerous toxicological and pharmacological studies of this compound to obtain information needed for diagnosis and treatment in the event of accidental UDMH exposure in man (refs 2, 3, 4, 16, 17, 24, 25, 26, 36). These studies have also been useful in setting safe threshold limit values, and in establishing proper propellant handling procedures.

Several of these investigations have shown that treatment with certain vitamin B₆ analogs in high doses will prevent convulsions and death in various laboratory animals exposed to known lethal concentrations of UDMH (refs 3, 8, 16, 24). The exact mechanism of this protection is not completely understood, but is believed to be primarily related to the function of pyridoxine as a co-enzyme for glutamic acid decarboxylase (GAD) and gamma aminobutyric acid transaminase (GABAT), in the gamma aminobutyric acid (GABA) shunt of the tricarboxylic acid cycle within the central nervous system (refs 8, 16).

The dose of pyridoxine required to successfully treat animals exposed to high concentrations of UDMH, as well as the suggested emergency treatment dose for severely exposed humans (ref 3), is much higher than the dose normally used in clinical practice. The purpose of this study is to briefly summarize pyridoxine toxicity studies in animals and to review the reported clinical uses of pyridoxine in high and/or prolonged doses in man, with regard to its possible toxic effects.

SECTION II

ANIMAL TOXICITY STUDIES

Few pyridoxine toxicity studies in animals have been reported in the literature (refs 3, 34, 35, 37). The results of these studies are summarized in tables I and II.

TABLE I
SUMMARY OF ACUTE TOXICITY STUDIES
OF
PYRIDOXINE IN LABORATORY ANIMALS

Animal	Investigator & Date	Compound Tested	Route of Administration	LD ₅₀ Dose mg/kg	Death
					Time from Dose*
Rats	Unna 1940	Pyridoxine Hydrochloride	Subcutaneous	3700	36-72 hr
	Unna 1940	"	Oral	5500-6000	36-72 hr
	Weigand 1940	"	iv	657	5 min
Mice	Weigand 1940	Pyridoxine Hydrochloride	iv	545	5 min
	Back 1963	Pyridoxamine dihydrochloride	ip	2100	24 hr

*Convulsions occurred before death under each condition.

TABLE II
SUMMARY OF CHRONIC TOXICITY STUDIES
OF
PYRIDOXINE IN LABORATORY ANIMALS

Animal	Investigator & Date	Compound Tested	Route of Administration	Dosage mg/kg/day	Duration* Days
Rats	Unna 1940	Pyridoxine hydrochloride	Oral	20	80
Mice	Weigand 1940	"	iv	100	14
Dogs	Unna 1940	"	Oral	20	80
Monkeys	Unna 1940	"	Oral	10	39
Monkeys	Unna 1940	"	Subcutaneous	10	106

*No clinical or pathological changes occurred subsequent to administration.

These data imply that pyridoxine toxicity, either acute or chronic, is relatively low in the species studied. Extrapolation of these findings to the clinical use of pyridoxine in humans suggests that a wide margin of safety exists between normal therapeutic doses and doses high enough to cause signs and symptoms of pyridoxine toxicity.

SECTION III

CLINICAL EXPERIENCE WITH MAN

Common Use and Dosage

Aside from its inclusion in small amounts in multivitamin preparations and its use in vitamin B₆ deficiencies, pyridoxine has been used in the treatment of many disorders for which no specific therapy is available, and in which the indications for pyridoxine are not well established. These include disorders such as the nausea and vomiting associated with pregnancy, motion sickness, post-anesthesia, and post-irradiation; acute alcoholic intoxication and delirium tremens; various dermatoses; anemias of certain types; and a variety of neuromuscular and neurological conditions.

The vitamin B₆ analog used almost exclusively in clinical practice is pyridoxine hydrochloride, since it is the form normally available to physicians. The usual adult doses range from 25 to 100 mg (occasionally up to 250 mg) daily, given either orally or parenterally. For a man weighing 70 kg, this is a dose range of 0.35 to 3.5 mg/kg/day.

Recommend Use in Acute UDMH Intoxication

To date, no human exposures to UDMH severe enough to cause convulsions have been reported, and pyridoxine in high doses has never been used for the treatment of acute UDMH toxicity in humans. Back, Pinkerton, and Thomas (ref 3) have recently recommended that an initial dose of pyridoxine hydrochloride of 25 mg/kg (25% given iv and 75% im) be administered parenterally at the first sign of significant UDMH toxicity (usually nausea or vomiting or both). They suggest a second dose of 25 mg/kg if convulsions occur and are at all severe or persistent.

Reported Clinical Use In High and/or Prolonged Doses

The literature from 1940 through June 1963 was surveyed. Twenty-four papers (11 U.S. and 13 foreign) were found in which were reported pyridoxine doses and/or duration of treatment to a degree sufficient to warrant inclusion in this review.

Only abstracts of the foreign papers were reviewed (these are noted in the list of references). Many of the U.S. papers reviewed in complete form did not contain all of the desired data, ie, numbers of subjects, ages, weights, sex, exact pyridoxine dose, routes, frequency and duration of administration, or methods used in evaluating possible toxic effects of pyridoxine. The purpose of the majority of articles reviewed was to evaluate the effectiveness of pyridoxine in various disorders, and not to study possible toxic side effects of the drug. Most of the 651 subjects reported in the 24 articles had active disease processes giving rise to a variety of symptoms, and positive physical examination and laboratory findings, all of which would complicate the detection of pyridoxine toxic effects were they to occur.

To aid in comparing the findings in these articles, the data were used to compute the milligram dose of pyridoxine per kilogram of body weight for each

study. The data available for these computations varied among the articles in completeness and specificity. The criteria used to calculate these mg/kg doses are given in table III. Accuracy of the computed mg/kg doses is believed to be reasonably reliable. The significant findings, including the calculated mg/kg doses, are given in table IV.

As shown in table IV, some subjects received large doses of pyridoxine in terms of usual clinical doses. However, harmful or toxic effects from the drug were not reported in any of the studies.

To determine the numbers of subjects receiving the drug, in single or total daily doses, at various dose levels, and by various routes, the data from the 24 studies were used as shown in table V. This information is helpful in regard to the relative safety of giving pyridoxine in high doses over a short period of time. The numbers of subjects are given cumulatively.

TABLE III

CRITERIA AND DATA USED TO COMPUTE PYRIDOXINE mg/kg
DOSES IN THE STUDIES REVIEWED

Dose of Pyridoxine (single or total daily dose)		Weight of Subjects		Age of Subjects				Criteria for mg/kg Computation	
				Known Adults	Known children				
					Age Known + 2 yr	Age Range Known > 2 yr	Age Un- known		
Exact	Dose Range	Known	Unknown					No.	Factors Used in Calculation
X		X						I	Known dose and weight.
X			X	X				II	Known dose and "stand- ard" 70 kg adult.
X			X		X			III	Known dose and average weight for closest year of age.
	X	X or	X	X or	X			IV	Known dose range and: (1) known weight; (2) 70 kg adult; or (3) average weight for closest year of age.
X or	X		X			X or	X	V	Known dose or dose range and arbitrarily selected, representative <u>stated</u> weight.

TABLE IV

REPORTED USES OF PYRIDOXINE HYDROCHLORIDE IN HIGH DOSES IN 651 HUMAN SUBJECTS

Reference	Subjects		Pyridoxine Hydrochloride Usage				mg/kg Dose (single or daily total***)	
	Description	No.	Purpose	Dose or Dose Range (mg)	Route* (P, O, or ?)	Dura- tion** (days, S or ?)	Calculated	Criteria
14	Adult diabetics M&F	144	B ₆ deficiency test	1000	P	S	14.3	II
14	" "	94	B ₆ deficiency therapy	500-1000	?	?	7.15-14.3	IV(2)
18	" "	27	Xanthuremic acid excre- tion study	500-600	O	5	7.15-8.6	IV(2)
22	Children w/anemias or 1-2 yr							
22	Dystrophies 0-1 yr	28	Therapy	80-100	O&P	14-21	8.0-9.0	IV(3)
12	INH poisoning-25 mo. M, 13.0 kg	76	"	40-80	O&P	14-21	6.0-10.0	IV(3)
		1	"	200	P (div, im)	S	15.4	I
12	21 mo. F, 11.4 kg	1	"	100	P (iv)	S	8.8	I
27	Adult M w/anemia	1	"	1000	O	30	14.3	II
29	Convulsions-3 mo, 6.7 kg	1	"	100	P (im)	S	15.0	I
20	Hemicconvulsive & hemiplegic children, ? ages	4	"	300-400	O&P	?	8.5-11.5 (35 kg)	V
21	Adults w/delirium tremens	14	Therapy/study	0-1000	?	?	0-14.3	IV(2)
10	Adults w/acute alcoo- holism	20	Therapy	500	P (iv)	7	7.15	II
13	Adult nursing mothers- ? number	1+	B ₆ enrichment of milk	500-1000	O	?	7.15-14.3	IV(2)
33	Children w/encephalo- pathies - ? ages	19	Therapy	300	P	30	8.5 (35 kg)	V
15	Phenylketonuric pts- ages: 8-13 yrs	5	Therapy	150	?	28	3.0-5.4	III
15	15-41 yrs	5	Therapy	150	?	28	2.1-2.6	IV(2)
32	Children w/pertussis encephalitis-? ages	3	Therapy	300	?	30	20.0 (15 kg)	V
9	Adults-17 normals, 5 hepatic pts	22	Glutamic acid metabolism study	500	?	10	7.15	II
1	Adults, M, acute	35	Therapy	1000	?	?	14.3	II

33	Children w/encephalopathies - ? ages	19	of milk Therapy	300	P	30	8.5 (35 kg) 3.0 - 5.4	V
15	Phenylketonuric pts- ages: 8-13 yrs	5	Therapy	150	?	28	2.1 - 2.6	III
15	Children w/pertussis ages: 15-41 yrs	5	Therapy	150	?	28	20.0	IV(2)
32	Children w/pertussis encephalitis-? ages	3	Therapy	300	?	30	(15 kg)	V
9	Adults-17 normals, 5 hepatic pts	22	Glutamic acid metabolism study	500	?	10	7.15	II
1	Adults, M, acute alcoholism	35	Therapy	1000	?	?	14.3	II
30	Adults, M, 2 normals, wts: both 71.5 kg	2	B ₆ therapy study	500	P(iv)	S	7.0	I
30	Adults, M, 6 alcoholics wts: 54.0 kg	1	B ₆ therapy study	500	P(iv)	S	9.3	I
30	" " " " " "	1	"	500	P(iv)	S	7.8	I
30	" " " " " "	1	"	1000	P(iv)	S	15.6	I
30	" " " " " "	1	"	1000	P(iv)	S	13.5	I
30	" " " " " "	1	"	1000	P(iv)	S	13.0	I
30	" " " " " "	1	"	2000	P(iv)	S	31.7	I
19	Adult, M, alcoholic	1	Therapy	1000	P(iv)	S	14.3	II
11	Adults, w/Parkinson's disease	20	Therapy	600-1400	O&P	?	8.6 - 20.0	IV(2)
5	Adult tbc pts on INH	21	Prevention and Therapy, INH	150- 450	?	70	2.1 - 6.4	IV(2)
28	Adults w/dermatoses	11	Therapy	300	P	28	4.3	II
28	Adults w/dermatoses	6	Therapy	600	P	28	8.6	II
28	Adults w/dermatoses	6	Therapy	600-1000	P	21	8.6 - 14.3	IV(2)
23	Infants w/erythroderma - ? ages	46	Therapy	30-50	P	3-21	5.0 - 8.0 (6 kg)	V
7	Adult nursing mothers- ? number	1+	Milk secretion stimulation	200- 900	?	?	3.6 - 7.15	IV(2)
6	13 adult normals: ? number adult pts w/ diabetes or myopathies	14+	Study on B ₆ effect on blood sugar	20- 800	P(iv)	S	0.3 - 11.4	IV(2)
31	Adults w/Parkinsonism	16	Therapy	250- 500	P(iv & im)	?	3.6 - 7.15	IV(2)
Total subjects		651						

*Route of Administration: P = parenteral
O = oral

? = not reported in the study

**Duration of treatment: Days listed in whole numbers, S = single dose
? = not reported in study

***Criteria: Refer to Table III for criteria used in computing mg/kg dosages.

2

TABLE V

CUMULATIVE NUMBERS OF SUBJECTS RECEIVING PYRIDOXINE
(SINGLE OR TOTAL DAILY DOSES) AS mg/kg DOSE LEVELS
AND BY VARIOUS ROUTES OF ADMINISTRATION

Dose mg/kg* Levels (single or total daily dose)	Cumulative Numbers of Subjects						
	All Subjects	Route of Administration					
		Unknown	Oral	Parenteral			
				Total	iv	im	Unknown
30 +	1	-	-	1	1	-	-
20 +	4	3	-	1	1	-	-
15 +	7	3	-	4	3	1	-
13 +	190	38	1	151	6	1	144
11 +	191	38	1	152	7	1	144
9 +	191	38	1	152	7	1	144
7 +	442	154	55	233	31	1	201
5 +	564	154	93	317	31	1	285
3 +	597	160	93	344	39	9	296
1 +	623	186	93	344	39	9	296
< 1	651	200	93	358	53	9	296

*mg/kg dose levels as computed in table IV.

The relative safety of giving pyridoxine at various dose levels is probably a lesser problem than short-term high dose safety. However, the data obtained in this review have been examined in terms of duration of treatment, various dose levels, and numbers of subjects. This cumulative information is given in table VI.

TABLE VI

CUMULATIVE NUMBERS OF SUBJECTS RECEIVING PYRIDOXINE
BY DURATION OF TREATMENT AT VARIOUS mg/kg DOSAGE LEVELS

Dose mg/kg* Levels (single or total daily dose)	Cumulative Numbers of Subjects							
	All Subjects	Duration of Treatment (in days)						
		<1	1-4	5-9	10-19	20-29	30+	Unknown
30+	1	1	-	-	-	-	-	-
20+	4	1	-	-	-	-	3	-
15+++	7	4	-	-	-	-	3	-
13+	190	151	-	-	-	-	4	35
11+	191	152	-	-	-	-	4	35
9+	191	152	-	-	-	-	4	35
7+	442	156	-	47	50	12	23	154
5+	564	156	46	47	126	12	23	154
3+	597	156	46	47	126	28	23	171
1+	623	156	46	47	126	33	44	171
<1	651	170	46	47	126	33	44	185

*mg/kg dosage levels as computed in table IV.

SECTION IV

CONCLUSION

A review of pyridoxine toxicity studies in animals suggests that both acute and chronic toxicity are relatively low in the species studied. This implies the existence of a very wide margin of safety between normal therapeutic doses and doses high enough to cause signs and symptoms of pyridoxine toxicity.

Analysis of the data on the clinical use of pyridoxine at high and/or prolonged doses suggests that pyridoxine toxicity, both acute and chronic, is low for man. It seems reasonable to believe that pyridoxine hydrochloride can be used safely in doses much higher than the usual clinical doses when required in the specific treatment of a clinical entity such as acute UDMH intoxication.

LIST OF REFERENCES

1. Atkinson, G. W. and W. C. Kappes: "Pyridoxine (Vitamin B₆) in Alcoholism," Virginia Med. Mo. 83: 391-93, September 1956.
2. Back, K. C., M. Pinkerton, A. Cooper and A. A. Thomas: "Absorption, Distribution, and Excretion of 1,1-Dimethylhydrazine," Toxicol. Appl Pharmacol. 5: 401-13, 1963.
3. Back, K. C., M. K. Pinkerton and A. A. Thomas: Therapy of Acute UDMH Intoxication, AMRL-TDR-63-44 (AD 411 759), Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, June 1963.
4. Back, K. C. and A. A. Thomas: "Pharmacology and Toxicology of 1,1-Dimethylhydrazine (UDMH)," Am. Ind. Hyg. Assoc. J. 24: 23-27, 1963.
5. Biehl, J. P. and R. W. Vilter: "Effect of Isoniazid on Vitamin B₆ Metabolism; Its Possible Significance in Producing Isoniazid Neuritis," Proc Soc Exp Biol Med 85: 389-92, March 1954.
6. Briskas, S, F. Delbarre and P. Desgrez: "Action of Pyridoxine on Blood Sugar in Normal Subjects and in Some Pathological Conditions," Compt Rend Soc Biol 140: 400-2, 1946 (Abstract).
7. Buccellato, T. and P. Gismondo: "Clinical Observations of an Anti-Galactogenic Effect of Large Doses of Vitamin B₆," Sicilia Sanit 3/7: 15-22, Palermo 1950 (Abstract).
8. Dubnick, B., G. A. Leeson, and C. C. Scott: "Effect of Forms of Vitamin B₆ on Acute Toxicity of Hydrazines," Toxicol Appl Pharmacol 2: 403-9, 1960.
9. Engelhardt-Gölkel, A., W. Seitz, and I. Woller: "Effect of Pyridoxine and Pyridoxal Phosphate on the Deamination of Glutamic Acid in Man," Klin Wschr 36/9: 409-11, 1958 (Abstract).
10. Ewing, J. A., "The First Phase of Alcohol Rehabilitation. Report of a Controlled Study with Benactyzine, Paraldehyde, and Pyridoxine," Quart J. Studies Alcohol ZI: 68-81, 1960.
11. Finke, H., "Treatment of the Parkinsonian Syndrome with Large Doses of Vitamin B₆," Munch Med Wochensch 96: 637-39, 1954 (Abstract).
12. Hyatt, H., "Acute Poisoning from Overdose of Isoniazid," Amer. J. Dis Child 102: 228-32, 1962.
13. Korlin, R., "Effect of Pyridoxine Administration on the Vitamin B₆ Activity of Human Milk," Bull. Soc. Chem Biol (Paris) 41: 1085-91, 1959 (Abstract).

14. Lebon, Jr., Claude R., M. Leutenegger, F. Gantz, P. Galley and J. Tricoire: "Vitamin B₆ Deficiency in Diabetes: Possible Role in Producing Degenerative Complications," Presse Med 69: 230-32, 1961 (Abstract).
15. McGeer, E. G. and B. Tischler: "Vitamin B₆ and Mental Deficiency. The Effects of Large Doses of B₆ (Pyridoxine) in Phenylketonuria," Canadian J. Biochem, 37/3: 485-91, 1959.
16. Meyers, F., F. Weir, G. Eisenlord, and J. Nemenzo: "Neuropharmacology of Hydrazine, UDMH, and Pentaborane," The Hine Labs Inc., sponsored by the Advanced Research Projects Agency, DOD, April 1963.
17. Mitz, M., F. Aldrich, and B. Vasta: Study of the Intermediary Metabolic Pathways of 1,1-Dimethylhydrazine, AMRL-TDR-62-110 (AD 290 509), Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, September 1962.
18. Montenegro, P.: "Pyridoxine and Diabetes," Acta Vitaminol 15: 55-60, 1961, (Abstract).
19. Palmer, E. J.: "Pyridoxine HCl in the Treatment of Acute Alcoholism and Delirium Tremens," Virginia Med Mo 85: 15-16, 1955.
20. Pena, J., "The Therapeutic Effect of Large Amounts of Vitamin B₆ on Hemiconvulsive and Hemiplegic Syndromes and Their Sequelae," Rev Espanola Pediat 16: 385-92, 1960 (Abstract).
21. Peters, U. H. and H. Neumann: "Vitamin B₆ Deficiency in Delirium Tremens," Arch Psychiat Nervenkrankh 201: 165-72, 1960.
22. Popova, D. N.: "Beneficial Effect of Vitamin B₆ on Blood Picture and Weight in Children with Signs of Hypotrophy and Secondary Anemia," Vop Pitan 20/6: 37-40, Pediat Med Inst., Leningrad 1961 (Abstract).
23. Parcelli, T.: "Therapeutic Actions of Certain Vitamins of the B Complex and of Embryo Preparations in Infantile Erythrodermia Desquamativa," Pediatrics 60: 56-62, 1952 (Abstract).
24. Reeves, J. L.: "Influence of Large Doses of Pyridoxine Hydrochloride on the Convulsive Activity of UDMH in Monkeys," SAM Report No. 62-31, USAF Aerospace Med. Ctr, Brooks Air Force Base, Texas, December 1961.
25. Reynolds, H., F. Rohles, V. Caster, H. Brunson, J. Prine, K. Back and A. Thomas: The Effect of UDMH Injection on Complex Avoidance Behavior in the Java Monkey, AMRL-TDR-63-39 (AD 410-933), Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, May 1963.
26. Reynolds, H., F. Rohles, J. Fineg, K. Back and A. Thomas: The Effect of UDMH Injection on Learned Behavior in the Java Monkey, AMRL-TDR-62-64 (AD 283 846), Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, June 1962.

27. Roab, S., A. Hant, G. Cartwright, and M. Wintrobe: "Pyridoxine-Responsive Anemia," Blood 18: 285-302, 1961.
28. Schreiner, A. W., E. Rockwell and R. W. Vilter: "A Local Defect in the Metabolism of Pyridoxine in the Skin of Persons with Sebarrheic Dermatitis of the Sicca Type," J. Invest Dermatol 19: 95-6, 1952.
29. Sriver, C. R., "Vitamin B₆ - Dependency and Infantile Convulsions," Pediatrics 26: 62-74.
30. Small, M. D., N. Zamcheck, J. J. Votale, A. Longarim, and B. Fisher: "The Effect of Pyridoxine Hydrochloride in Acute Alcoholic Intoxication," J. Lab Clin Med 46: 12-20, 1955.
31. Stefanini, M. and G. Roi: "Preliminary Results of Treatment of Post-encephalitic Parkinsonism with Pyridoxine," Gazzetta Sanitaria 19/7-8: 171-73, 1948 (Abstract).
32. Suarez, M.: "Treatment of Whooping Cough, with Special Reference to the Use of Vitamin B₆ in the Central Syndrome," Rev Espanola Pediat 14: 77-83, 1958 (Abstract).
33. Suarez, M., J. Teixeira, and G. Sierra: "Clinical and Bio-electric Study of the Action of Vitamin B₆ in Congenital Encephalopathy," Rev Espanola Pediat 14: 57-62, 1958 (Abstract).
34. Unna, K.: "Studies on the Toxicity and Pharmacology of Vitamin B₆," J. Pharmacol 70: 400-7, 1940.
35. Unna, K and W. Antopol: "Toxicity of Vitamin B₆," Proc. Soc. Exp. Biol Med 43: 116-18, 1940.
36. Weeks, M., G. Maxey, M. Sicks and E. Greene: "Vapor Toxicity of UDMH in Rats and Dogs from Short Exposures," Am. Ind. Hyg Assoc J 24: 137-43, 1963.
37. Weigand, C., C. Eckler and K. Chen: "Action and Toxicity of Vitamin B₆ Hydrochloride," Proc Soc Exp Biol Med 44: 147-51, 1946.

UNCLASSIFIED
Security Classification

DOCUMENT CONTROL DATA - R&D <small>(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)</small>		
ORIGINATING ACTIVITY (Corporate author) Aerospace Medical Research Laboratories, Aerospace Medical Division, Air Force Systems Command, Wright-Patterson Air Force Base, Ohio		2a. REPORT SECURITY CLASSIFICATION <div style="text-align: center; border: 1px solid black; padding: 2px;">UNCLASSIFIED</div> 2b GROUP <div style="text-align: center; border: 1px solid black; padding: 2px;">N/A</div>
3. REPORT TITLE <div style="text-align: center; padding: 10px 0;">PYRIDOXINE (VITAMIN B₆) TOXICITY LITERATURE REVIEW</div>		
4. DESCRIPTIVE NOTES (Type of report and inclusive dates) <div style="text-align: center; padding: 5px 0;">Review (literature from 1940 through June 1963)</div>		
5. AUTHOR(S) (Last name, first name, initial) <div style="text-align: center; padding: 10px 0;">Schneider, Robert A., Captain, USAF, MC, FS</div>		
6. REPORT DATE <div style="text-align: center; padding: 5px 0;">October 1964</div>	7a. TOTAL NO. OF PAGES <div style="text-align: center; padding: 5px 0;">17</div>	7b. NO. OF REFS <div style="text-align: center; padding: 5px 0;">37</div>
8a. CONTRACT OR GRANT NO. b. PROJECT NO 6302 c. Task No. 630202 d.		9a. ORIGINATOR'S REPORT NUMBER(S) <div style="text-align: center; padding: 10px 0;">AMRL-TR-64-106</div> <hr/> 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)
10. AVAILABILITY/LIMITATION NOTICES Qualified requesters may obtain copies of this report from DDC. Available, for sale to the public, from the Office of Technical Services, U.S. Department of Commerce, Washington, D. C. 20230.		
11. SUPPLEMENTARY NOTES Prepared in partial fulfillment of the Phase III requirements for residency in Aviation Medicine.		12. SPONSORING MILITARY ACTIVITY Aerospace Medical Research Laboratories, Aerospace Medical Division, Air Force Systems Command, Wright-Patterson AFB, O.
13. ABSTRACT The literature from 1940 through June 1963 was surveyed to summarize the data from pyridoxine toxicity studies in animals and to ascertain the highest doses of pyridoxine (vitamin B ₆ analogs) that have been administered to human subjects as a therapeutic measure with no clinical evidence of toxicity. Analysis of the data indicated that doses of 25 mg/kg pyridoxine hydrochloride should be well tolerated as a therapeutic measure when required. In particular, pyridoxine hydrochloride can be used when required in the specific treatment of a clinical entity such as acute UDMH intoxication.		

UNCLASSIFIED
Security Classification

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Toxicity, toxicology Pharmacology Pyridoxine Dosage, biology Toxic tolerances, toxicology Vitamin B complex, pyridoxine Animals Man 1,1-dimethylhydrazine (UDMH) toxicity						

INSTRUCTIONS

1. ORIGINATING ACTIVITY: Enter the name and address of the contractor, subcontractor, grantee, Department of Defense activity or other organization (*corporate author*) issuing the report.

2a. REPORT SECURITY CLASSIFICATION: Enter the overall security classification of the report. Indicate whether "Restricted Data" is included. Marking is to be in accordance with appropriate security regulations.

2b. GROUP: Automatic downgrading is specified in DoD Directive 5200.10 and Armed Forces Industrial Manual. Enter the group number. Also, when applicable, show that optional markings have been used for Group 3 and Group 4 as authorized.

3. REPORT TITLE: Enter the complete report title in all capital letters. Titles in all cases should be unclassified. If a meaningful title cannot be selected without classification, show title classification in all capitals in parenthesis immediately following the title.

4. DESCRIPTIVE NOTES: If appropriate, enter the type of report, e.g., interim, progress, summary, annual, or final. Give the inclusive dates when a specific reporting period is covered.

5. AUTHOR(S): Enter the name(s) of author(s) as shown on or in the report. Enter last name, first name, middle initial. If military, show rank and branch of service. The name of the principal author is an absolute minimum requirement.

6. REPORT DATE: Enter the date of the report as day, month, year; or month, year. If more than one date appears, on the report, use date of publication.

7a. TOTAL NUMBER OF PAGES: The total page count should follow normal pagination procedures, i.e., enter the number of pages containing information.

7b. NUMBER OF REFERENCES: Enter the total number of references cited in the report.

8a. CONTRACT OR GRANT NUMBER: If appropriate, enter the applicable number of the contract or grant under which the report was written.

8b, 8c, & 8d. PROJECT NUMBER: Enter the appropriate military department identification, such as project number, subproject number, system numbers, task number, etc.

9a. ORIGINATOR'S REPORT NUMBER(S): Enter the official report number by which the document will be identified and controlled by the originating activity. This number must be unique to this report.

9b. OTHER REPORT NUMBER(S): If the report has been assigned any other report numbers (*either by the originator or by the sponsor*), also enter this number(s).

10. AVAILABILITY/LIMITATION NOTICES: Enter any limitations on further dissemination of the report, other than those

imposed by security classification, using standard statements such as:

- (1) "Qualified requesters may obtain copies of this report from DDC."
- (2) "Foreign announcement and dissemination of this report by DDC is not authorized."
- (3) "U. S. Government agencies may obtain copies of this report directly from DDC. Other qualified DDC users shall request through _____."
- (4) "U. S. military agencies may obtain copies of this report directly from DDC. Other qualified users shall request through _____."
- (5) "All distribution of this report is controlled. Qualified DDC users shall request through _____."

If the report has been furnished to the Office of Technical Services, Department of Commerce, for sale to the public, indicate this fact and enter the price, if known.

11. SUPPLEMENTARY NOTES: Use for additional explanatory notes.

12. SPONSORING MILITARY ACTIVITY: Enter the name of the departmental project office or laboratory sponsoring (*paying for*) the research and development. Include address.

13. ABSTRACT: Enter an abstract giving a brief and factual summary of the document indicative of the report, even though it may also appear elsewhere in the body of the technical report. If additional space is required, a continuation sheet shall be attached.

It is highly desirable that the abstract of classified reports be unclassified. Each paragraph of the abstract shall end with an indication of the military security classification of the information in the paragraph, represented as (TS), (S), (C), or (U).

There is no limitation on the length of the abstract. However, the suggested length is from 150 to 225 words.

14. KEY WORDS: Key words are technically meaningful terms or short phrases that characterize a report and may be used as index entries for cataloging the report. Key words must be selected so that no security classification is required. Identifiers, such as equipment model designation, trade name, military project code name, geographic location, may be used as key words but will be followed by an indication of technical context. The assignment of links, rules, and weights is optional.